Amendments to the Specification

Please replace the paragraph that appears from page 1, line 18 to page 2, line 3 with the following replacement paragraph:

> Insulin resistance, which is commonly associated with prevalent type 2 diabetes, is a state in which target cells fail to respond to normal levels of circulating insulin. *See, e.g.* Saltiel *et al., Nature 414:* 799-806 (2001). This lack of response, in turn, results in hyperinsulinemia to compensate for the resistance to insulin in the prediabetic state. Subsequently, hyperglycemia develops due to the failure of the pancreatic beta cells to produce and secrete enough insulin to compensate for the imbalance in glucose metabolism. Type 2 diabetes is the most common form of the disease, affecting 16 million people in the United States alone. (Source: American Diabetes Association~~, www.diabetes.org~~). Roughly one-third of these people remain undiagnosed. (Source: id.)

Please replace the paragraph that appears from page 10, line 20 to page 11, line 3 with the following replacement paragraph:

> The newly identified Ser1101 phosphorylation site was identified/predicted by analyzing the human IRS-1 amino acid sequence with the ScanSite program ~~(http://scansite.mit.edu)~~ (*see ~~also~~* Yaffe *et al.*, *Nat Biotechnol. 19(4):* 348-53 (2001)). This algorithm searches for motifs within proteins that are likely to be phosphorylated by specific protein kinases or bind to domains such as SH2 domains, 14-3-3 domains or PDZ domains. Optimal phosphorylation sites for particular serine/threonine protein kinases or tyrosine protein kinases are predicted using a matrix of selectivity values for amino acids at each position relative to the phosphorylation site, as determined from the oriented peptide library technique described by Songyang *et al.*, Current Biology 4: 973-982 (1994) and Songyang *et al.*, Nature 373: 536-539 (1995).